

WEST

End of Result Set

 [Generate Collection](#) [Print](#)

L16: Entry 15 of 15

File: USPT

Feb 6, 1990

DOCUMENT-IDENTIFIER: US 4898932 A

TITLE: Monoclonal antibodies reactive with activated and oncogenic ras p21 proteins

Abstract Text (1):

Monoclonal antibodies reactive with oncogenic and activated ras p21 proteins containing glutamic acid, arginine or valine at position 12 and unreactive with normal ras p21 proteins containing glycine at position 12. The antibodies are secreted by hybridomas obtained by immunizing mice with synthetic dodecapeptides corresponding in amino acid sequence to positions 5-16 of normal ras p21 proteins, except having glutamic acid, arginine or valine in place of glycine at position 12. The antibodies and Fab fragments thereof are useful for diagnosis, staging and classification of malignant and premalignant lesions.

Application Filing Date (1):

19871022

Detailed Description Text (23):

Monoclonals antibodies E170, E184, R256 and DWP specifically react with activated ras proteins in malignant cells and do not react with ras proteins found in normal cells. Therefore, these monoclonal antibodies will be useful in the differentiation of normal and neoplastic cell in various immunological and biochemical assays. Secondly, these antibodies will permit the classification of neoplastic cells into various categories based on the particular ras protein expressed. These antibodies will be useful therefore in the quantitation of activated ras proteins which in turn will be useful in staging tumors based on levels of ras p21 expression. Thus, better diagnosis of malignant cells, the ability to differentiate malignant from premalignant cells and the ability to classfiy malignant cells into various categories due to levels of ras expression will result from the application of monoclonal antibodies E170, E184, R256 and DWP.

WEST

 [Generate Collection](#) [Print](#)

L16: Entry 3 of 15

File: USPT

Nov 13, 2001

DOCUMENT-IDENTIFIER: US 6316208 B1

** See image for Certificate of Correction **

TITLE: Methods for determining isolated p27 protein levels and uses thereof

Application Filing Date (1):
19970203

Detailed Description Text (84):

Detection of p27 stability may serve as a marker for the presence of cancerous cells and also allow for determination of the prognosis of the patient carrying the tumor. The subject method can be used to augment the detection and/or prognosis of such solid tumors as, for example, carcinomas (particularly epithelial-derived carcinomas) of such tissues as ovaries, lung, intestinal, pancreas, prostate, testis, liver, skin, stomach, renal, cervical, colorectal, and head and neck; melanomas; and sarcomas such as Kaposi's sarcoma and rhabdomyosarcoma. In preferred embodiments, the subject method is used to assess a malignant or pre-malignant epithelial carcinoma.

5
6
7

WEST

End of Result Set

 [Generate Collection](#) [Print](#)

L19: Entry 4 of 4

File: USPT

Nov 16, 1999

DOCUMENT-IDENTIFIER: US 5984882 A

TITLE: Methods for prevention and treatment of cancer and other proliferative diseases with ultrasonic energy

Application Filing Date (1):19971216Detailed Description Text (19):

Overexpression of growth factors leads to suppression of cell death and has significant implications in the treatment of cancer. For example, the growth and proliferation of epithelial cells in prostate cancer is influenced by EGF, TGF-alpha, TGF-beta, NGF and FGF. The overexpression of these growth factors prevents DNA fragmentation and apoptotic mechanism (Chung, L. W. et al., 1992, J. Cell Biochem. Supplm. 16H:99-105). The methods of the present invention can induce apoptosis of growth factor receptor-bearing precancerous and cancerous cells and supporting stromal cells with ultrasonic energy.

WEST

 [Generate Collection](#) [Print](#)

L19: Entry 1 of 4

File: USPT

Oct 29, 2002

DOCUMENT-IDENTIFIER: US 6472376 B2

** See image for Certificate of Correction **

TITLE: Suppression of malignancy utilizing ribonucleotide reductase R1

Application Filing Date (1):
19980924Brief Summary Text (8):

Regulation of ribonucleotide reductase, and particularly the R2 component, is markedly altered in malignant cells exposed to tumor promoters or to the growth factor TGF-.beta. [Amara, et al., 1994; Chen et al., 1993; Amara et al., 1995b; Hurta and Wright, 1995; Hurta et al., 1991]. An R1 deletion can be detected in some human colorectal carcinomas [Glenney, 1986]. Higher levels of enzyme activity have been observed in cultured malignant cells when compared to nonmalignant cells [Weber, 1983; Takeda and Weber, 1981; Wright et al., 1989a], and increased levels of R2 protein and R2 mRNA have been found in pre-malignant and malignant tissues as compared to normal control tissue samples [Saeki et al., 1995; Jensen et al., 1994]. Regulation of ribonucleotide reductase, and in particular the R2 component, is significantly elevated in transformed cells exposed to tumor promoters, or to transforming growth factor .beta. in growth factor mediated mechanisms of tumor progression [Amara et al., 1996; Chen et al., 1993; Amara et al., 1995b].

Detailed Description Text (64):

References Amara et al., 1994. Phorbol ester modulation of a novel cytoplasmic protein binding activity at the 3'-untranslated region of mammalian ribonucleotide reductase R2 mRNA and role in message stability. J. Biol. Chem. 269:6709-7071. Amara et al., 1995A. Altered regulation of message stability and tumor promoter-responsive cis-trans interactions of ribonucleotide reductase R1 and R2 messenger RNAs in hydroxyurea-resistant cells. Cancer Res. 55:4503-4506. Amara et al., 1995B. Defining a novel cis element in the 3'-untranslated region of mammalian ribonucleotide reductase component R2 mRNA: Role in transforming growth factor-.beta..sub.1 induced mRNA stabilization. Nucleic Acids Res. 23:1461-1467. Amara et al. 1996. Defining a novel cis-element in the 3'-untranslated region of mammalian ribonucleotide reductase component R2 mRNA: cis-trans interactions and message stability. J. Biol. Chem. 271:20126-20131. Ashihara and Baserga, 1979. Cell Synchronization. Methods Enzymol. 58:248-262. Betz et al., 1994, Basic Neurochem. Molecular Cell, (Raven Press Ltd, New York) 5th Ed., 681-699 Bickel, et al., 1993, "Pharmacologic effects in vivo in brain by vector-mediated peptide drug delivery" Proc. Natl. Acad. Sci. USA 90(7)2618-2622 Blaesse, 1997. Gene Therapy for Cancer. Scientific American 276(6):111-115. Bjorklund, et al., 1990. Biochemistry, 29:5452-5458 Bjorklund et al., 1993. Structure and promoter characterization of the gene encoding the large subunit (R1 Protein) of mouse ribonucleotide reductase. Proc. Natl. Acad. Sci. USA 90:11322-11326. Brem et al., "Polymers as controlled drug delivery devised for the treatment of malignant brain tumors" Eur. J. Pharm. Biopharm 39:2-7 (1993) Capecchi, "Altering the genome by homologous recombination" Science 244:1288-1292 (1989). Caras, et al 1985. Cloned Mouse Ribonucleotide Reductase Subunit M1 cDNA Reveals Amino Acid Sequence Homology with Escherichia coli and Herpesvirus Ribonucleotide Reductases. Biol Chem. 260:7015-7022. Chan et al., 1993. Phosphorylation of ribonucleotide reductase R2 protein: in vivo and in vitro evidence of a role for p.delta.4.sup.cdc2 and CDK2 protein kinases. Biochemistry 32:12835-12840. Chen et al., 1993. Mammalian ribonucleotide reductase R1 mRNA stability under normal and phorbol ester stimulating conditions: involvement of a cis-trans interaction at the 3'-untranslated region. EMBO J., 12:3977-3986. Chen et al., 1994A. Regulation of mammalian ribonucleotide reductase R1 mRNA stability is mediated by a ribonucleotide reductase R1 mRNA 3'-untranslated region cis-trans interaction through a protein kinase C-controlled pathway. Biochem. J. 302:125-132.

Chen et al., 1994B. Defining a novel ribonucleotide reductase R1 mRNA *cis* element that binds to an unique cytoplasmic trans-acting protein. *Nucleic Acids Res.*, 22:4796-4797.

Choy et al., 1988. Molecular mechanisms of drug resistance involving ribonucleotide reductase: hydroxyurea resistance in a series of clonally related mouse cell lines selected in the presence of increasing drug concentrations. *Cancer Res.* 48:2029-2035.

Culver, 1998. Site-Directed recombination for repair of mutations in the human ADA gene. (Abstract) *Antisense DNA & RNA based therapeutics*, February, 1998, Coronado, Calif.

Davis et al., 1994. Purification, Characterization, and Localization of Subunit Interaction Area of Recombinant Mouse Ribonucleotide Reductase R1 Subunit. *Biol. Chem.* 269:23171-23176.

Egan, et al., 1987A. Expression of H-ras Correlates with Metastatic Potential: Evidence for Direct Regulation of the Metastatic Phenotype in 10T1/2 and NIH 3T3 Cells. *Mol. Cell. Biol.* 7:830-837.

Egan et al., 1987B. Transformation by oncogenes encoding protein kinases induces the metastatic phenotype. *Science* 238:202-205.

Eriksson et al., 1984. Cell cycle-dependent regulation of mammalian ribonucleotide reductase. The S phase-correlated increase in subunit M2 is regulated by de novo protein synthesis. *J. Biol. Chem.* 259:11695-11700.

Fan et al., 1996A. Ribonucleotide reductase R2 component is a novel malignancy determinant that cooperates with activated oncogenes to determine transformation and malignant potential. *Proc. Natl. Acad. Sci. USA* 93:14036-14040.

Fan et al., 1996B. A link between ferritin gene expression and ribonucleotide reductase R2 protein, as demonstrated by retroviral vector mediated stable expression of R2 cDNA. *FEBS Lett.* 382:145-148.

Fan et al., 1996C. Cloning of a gene from *Chlamydia trachomatis* that complements thymidylate synthase-deficient *Escherichia coli*. In: *Abstracts of the 94th General Meeting of the American Society for Microbiology*, p. 134.

Filatov et al., 1996. Induction of the mouse ribonucleotide reductase R1 and R2 genes in response to DNA damage by UV light. *J. Biol. Chem.* 271:23698-23704.

Gilboa et al., 1986. Transfer and expression of cloned genes using retroviral vectors. *BioTechniques* 4(6):504-512.

Gingras, et al., 1991. *Cancer Res.* 50:4061-4066.

Glenney, 1986. *Anal. Biochem.* 79:4002-4005.

Goding, 1978. *J. Immunol. Methods* 20:241-253.

Hanania, et al 1995. Recent advances in the application of gene therapy to human disease. *Am. J. Med.* 99:537.

Huang et al., 1995. Multiple effects on drug sensitivity, genome stability and malignant potential by combinations of H-ras, c-myc and mutant p53 gene overexpression. *Int. J. Oncol.* 7:57-63.

Hurta, et al., 1991. Early induction of ribonucleotide reductase gene expression by transforming growth factor .beta..sub.1 in malignant H-ras transformed cell lines. *J. Biol. Chem.* 266:24097-24100.

Hurta and Wright, 1992. *J. Biol. Chem.* 267:7066-7071.

Hurta and Wright, 1994. Alterations in the cyclic AMP signal transduction pathway regulating ribonucleotide reductase gene expression in malignant H-ras transformed cell lines. *J. Cell. Physiology* 158:187-197.

Hurta and Wright, 1995. Malignant transformation by H-ras results in aberrant regulation of ribonucleotide reductase gene expression by transforming growth factor-.beta..sub.1. *J. Cell. Biochem.* 57:543-556.

Jensen et al., 1994. Identification of genes expressed in premalignant breast disease by microscopy-directed cloning. *Proc. Natl. Acad. Sci. USA*. 91:9257-9261.

Johnson and Bird, 1991 "Construction of single-chain FvB derivatives of monoclonal antibodies and their production in *Escherichia coli* in Methods in Enzymology (J J Langone, ed.; Academic Press, New York, N.Y.) 203:88-99.

Kempe, et al., 1976. *Cell* 9:541-550.

Kozak, 1987. *Nucleic Acids Res.* 20:8125-8148.

Lewis et al., 1978. Assay of ribonucleotide reduction in nucleotide-permeable hamster cells. *J. Cell Physiol.* 94:287-298.

Leonhardt, et al., Cell 71: 865-873.

Mader, et al., 1996. Proceedings of the Eighty-seventh Annual Meeting, American Association of Cancer Research 37:547.

Mann et al., 1988. Ribonucleotide reductase M1 subunit in cellular proliferation, quiescence, and differentiation. *J. Cancer Res.* 48:5151-5156.

Mann, et al., 1991. *Biochemistry* 30:1939-1947.

McClarty et al., 1990. Increased ferritin gene expression is associated with increased ribonucleotide reductase gene expression and the establishment of hydroxyurea resistance in mammalian cells. *J. Biol. Chem.* 265:7539-7547.

Miller et al., 1993. Use of retroviral vectors for gene transfer and expression. *Meth. Enzymol.* 217:581-599.

Pardridge, et al., 1992, "Blood-brain barrier and new approaches to brain drug delivery" *West J. Med.* 156(3) 281-286

Pardridge, 1992, "Recent Developments in peptide drug delivery to the brain" *Pharm. Toxicol.* 71(1):3-10

Quinn, et al., 1979. *Cancer Res.* 39:4914-4924.

Reichard, 1993. From RNA to DNA, why so many ribonucleotide reductases? *Science* 60:1773-1777.

Saeki et al., 1995. Immunohistochemical detection of ribonucleotide reductase in human breast tumors. *Int. J. Oncol.* 6:523-529.

Spearman et al., 1994. Antisense oligodeoxyribonucleotide inhibition of TGF-.beta..sub.1 gene expression and alterations in the growth and malignant properties of mouse fibrosarcoma cells. *Gene* 149:25-29.

Stubbe, 1989. Protein radical involvement in biological catalysis? *Annu. Rev. Biochem.* 58:257-285.

Taylor et al., 1992. Evidence for synergistic interactions between ras, myc and a mutant form of p53 in cellular transformation and tumor dissemination. *Oncogene* 7:1383-1390.

Thelander et al., 1985. Subunit M2 of mammalian ribonucleotide reductase. Characterization of a homogeneous protein isolated from M2-overproducing mouse cells. *J. Biol. Chem.* 260:2737-2741.

Thelander et al., 1980. Ribonucleotide reductase from calf thymus. Separation of the enzyme into two nonidentical subunits, proteins M1 and M2. *J. Biol. Chem.* 255:7426-7432. Thelander and Berg, 1986. *Mol. Cell. Biol.* 6:3433-3442. Thelander, et al 1990. *J. Biol. Chem.* 255:7624-7432 Tonin et al., 1987. Chromosomal assignment of amplified genes in hydroxyurea resistant hamster cells. *Cytogenet. Cell Genet.* 45:102-108. Weber, 1983. Biochemical strategy of cancer cells and the design of chemotherapy. *Cancer Res.* 43:3466-3492. Wright & Anazodo, 1996. Antisense Molecules and Their Potential For The Treatment Of Cancer and AIDS. *Cancer J.* 8:185-189. Wright, 1989A. Altered mammalian ribonucleotide reductase from mutant cell lines. *Encycl. Pharmacol. Therapeut.* 128:89-111. Wright, et al., 1989B Hydroxyurea and related compounds in Drug Resistance in Mammalian Cells. R. S. Gupta Ed. (CRC Press, Boca Raton, Fla., 1989), Vol. 1, pp 15-27. Wright et al., 1990A. Regulation and drug resistance mechanisms of mammalian ribonucleotide reductase and the significance to DNA synthesis. *Biochem. Cell Biol.* 68:1364-1371. Wright,et al., 1990b *Anticancer Res.* 10:1247-1256. Wright et al., 1993. Transforming growth factor .beta. and fibroblast growth factor as promoters of tumor progression to malignancy. *Crit. Rev. Oncogen.* 4:473-492.